EXHIBIT 12

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REBUTTAL REPORT OF ALAN DUCATMAN, M.D.

In the case of Sullivan, et al. v. Saint-Gobain Performance Plastics Company, No. 5:16-cv-000125-GWC (D. Vt.)

I. Introduction

This rebuttal report is offered to respond to certain contentions advanced by defendant's experts Philip S. Guzelian, M.D., Jeffrey H. Mandel, MD, MPH, and Edward J. Calabrese, PhD ("defendant's experts") in reports submitted in May of 2018, and is in addition to my prior two expert reports submitted in this matter, dated September 1, 2017 and December 15, 2017. In my previous reports, I discussed that members of the Bennington Exposure Class, as a result of ingesting drinking water from wells contaminated with Perfluorooctanoic acid ("PFOA") at levels in excess of pertinent health standards, have above-background levels of PFOA in their blood serum. This elevated PFOA exposure causes this population to suffer from an increased risk of development of certain PFOA-related illness or disease as compared to the background population, and I have previously stated that it is clinically necessary and appropriate to implement and administer a medical monitoring program for this exposed population in order to minimize disease and improve health outcomes. Additionally, I have provided specific recommendations as to the clinically appropriate design and implementation of a medical monitoring program in Bennington.

Defendant's experts are critical of my decision to recommend medical monitoring for the Bennington Exposure Class, and Dr. Guzelian, primarily, attempts to discredit this and other of my opinions by attacking the methods I utilized to form them. Therefore, the primary focus of this rebuttal report is to respond to Dr. Guzelian's unfounded criticisms of my methodology as well as his mischaracterizations and criticisms of my proposed Bennington medical monitoring program. As to other arguments made by defendant's experts, including those about the purported lack of toxicity of PFOA generally and the lack of general causation at above-background levels, as well

as dose-response and related arguments, to the extent not directly addressed herein, I rely on the opinions contained in my previous reports as well as the opinions contained in the expert rebuttal report of Dr. Philippe Grandjean.

II. Materials Reviewed

In preparing this rebuttal report, in addition to the materials referenced in my first two reports, I have reviewed the following: expert report of Philip S. Guzelian, MD; expert report of Jeffrey H. Mandel, MD, MPH; expert report of Edward J. Calabrese, PhD; and the expert rebuttal report of Philippe Grandjean, MD, DMsc. Additional references for this rebuttal report are provided below.

III. Rebuttal Opinions

A. Dr. Guzelian's Criticisms of my Methodology are Unfounded and Based on an Unconventional Approach to Risk Assessment and Causality.

Dr. Guzelian asserts that certain of my opinions in this matter are the product of "deep methodological flaws" (Guzelian, at 3). Specifically, Dr. Guzelian takes issue with: (1) my recommendation for medical monitoring of the Bennington Exposure Class, which he contends is flawed due to an alleged lack of use of "objective, quantifiable medical decision-making criteria" or principles of "evidence-based decision making"[1] (Guzelian, at 9, 12); and (2) my opinion that members of the Bennington Exposure Class suffer from an increased risk of specific PFOA-related disease due to their above-background PFOA-exposures, which he argues was the result of "cherry-picking" from the literature (Guzelian, at 13). Importantly, the underlying basis for Dr. Guzelian's critiques of my methodology is his interpretation of principles of evidence-based

[1] The peer literature has strongly criticized the misleading conflation of principles of EBT as presented by Dr. Guzelian and those of evidence based medicine, as these methodologies are considered fundamentally in conflict. Ruden C, Hansson SO. 2008. Evidence-based toxicology: "Sound science" in new disguise. International journal of occupational and environmental health 14:299-306.

toxicology ("EBT"), as demonstrated by his repeated, self-referential citations to his own 2005 article on EBT. EBT, and Dr. Guzelian's interpretations of it, have been the subject of much criticism in the peer literature, including the critique that EBT is "implausible and not mainstream when considered in relation to well-established principles in toxicological risk assessment" (Ruden and Hansson 2008). Importantly, as discussed in the expert rebuttal report of Dr. Grandjean, Dr. Guzelian's arguments in this matter related to medical monitoring would defeat the primary purpose of medical monitoring – the early detection of disease – by requiring unrealistic and additional evidence – essentially "observing the occurrence of the exposure-related disease" – prior to the implementation of medical monitoring.[2]

1. My Recommendation for Medical Monitoring of the Bennington Exposure Class is based on Application of Clinical Standards of Care to Compelling Evidence of Both Exposure and Internal Human Contamination.

Dr. Guzelian's claim that my decision to recommend medical monitoring in this matter is not based on any objective evidence is facially invalid. As is clear from my previous reports, my recommendation for medical monitoring of the Bennington Exposure Class is based on my perspective as a clinician faced with compelling evidence of human exposure to PFOA, a proven hazardous substance, coupled with corroborating evidence of internal human contamination and associated harm. Based on generally accepted standards of clinical care, which dictate that at-risk populations be monitored and evaluated, and the compelling evidence of human exposure and internal contamination, I recommended medical monitoring for members of the Exposure Class.

The exposed Bennington population has overwhelmingly strong evidence of exposure (via contaminated drinking water), as well as strong corroborating evidence of internal human

[2] Expert Rebuttal Report of Dr. Grandjean, at 69-70.

contamination in serum (via blood tests).[3] In terms of scientific evidence, this is known as a "completed exposure pathway,"[4] as the toxic exposure is certain, as opposed to merely potential. Given this well-documented evidence, and my application of accepted clinical standards of care, my decision to recommend medical monitoring was in fact based on objective, quantifiable medical decision-making criteria. I further note that my recommendation for medical monitoring of this exposed population is also consistent with the mainstream literature concerning medical monitoring programs that have been implemented, (Wones et al. 2009), general principles of medical monitoring contained in the peer literature, (Dobrow et al. 2018), as well as applicable regulatory guidance, including the criteria contained in the U.S. Agency for Toxic Substances and Disease Registry's ("ATSDR") Final Criteria for Determining the Appropriateness of a Medical Monitoring Program under CERCLA[5] and guidance issued by the Occupational Safety and Health Administration ("OSHA").[6]

It is completely inappropriate for Dr. Guzelian to attempt to substitute his own interpretation of principles of EBT for my clinical decision-making. My conventional decision-making stands in stark contrast to Dr. Guzelian's views of medical monitoring, under which he demands additional and unrealistic evidence that he contends is necessary to demonstrate efficacy of the program prior to its implementation. These views are not widely-accepted and have not been utilized by regulatory agencies and other bodies engaged in real-world risk assessment. As discussed above, Dr. Guzelian's unrealistic demands would likely necessitate years of additional

[3] Vermont Department of Health: Exposure to PFOA in Bennington and North Bennington Vermont: Results of Blood Testing and Exposure Assessment (Sept. 2017).
[4] ATSDR. Glossary of Terms. Available on Line at https://www.atsdr.cdc.gov/glossary.html
[5] Federal Register Vol. 60, No. 145, Friday July 28, 1995: ATSDR's Final Criteria for Determining the Appropriateness of a Medical Monitoring Program Under CERCLA. Available at https://www.gpo.gov/fdsys/pkg/FR-1995-07-28/pdf/95-18578.pdf.
[6] OSHA: Medical Screening and Surveillance Requirements in OSHA Standards, available at https://www.osha.gov/Publications/osha3162.pdf

study of exposed Bennington residents (and potentially others) in order to satisfy Dr. Guzelian's requirements of efficacy and benefits. The irony is that acceptance of such a "research-first" approach is that it would defeat the primary early detection purpose of medical monitoring in the first instance; and, it plainly is not clinically or medically acceptable for the members of the Bennington Exposure Class, who have been unknowingly exposed to PFOA, a known hazardous substance, through contamination of their private drinking water wells.

Monitoring is Appropriate on a Population Basis

Additionally, as discussed in detail in my first expert report, which is incorporated herein, my recommendation for monitoring is also clinically appropriate on a class-wide, i.e., population basis, irrespective of any individualized considerations or differences as contended by Dr. Guzelian (Guzelian, at 21). Dr. Guzelian places much emphasis on the individualities that are demonstrated by the medical records of the named plaintiffs (which to my understanding were obtained to look for other sources of PFOA exposure). Although any member of the Exposure Class may have the normal human condition of varying susceptibilities, pre-existing health conditions, and other factors that could increase that individual's background risk of developing PFOA-related disease, the commonality shared by every member of the Exposure Class is the increased risk of PFOA-related illness or disease caused by their above-background PFOA exposures. Given these common exposures, medical monitoring should be implemented on a class-wide basis, despite any individualized considerations, as the increased risk of disease is shared across this population without regard to any such considerations.

My conclusion in this regard is consistent with the applicable regulatory guidance, including that of the ATSDR referenced above, which deals exclusively with monitoring programs

implemented and administered on a community-wide basis.[7] ATSDR is clear that medical monitoring is appropriate for a "target community," and that such monitoring is based on exposure as well as the potential for an increased risk of disease – irrespective of any individualized considerations:

> Within this framework, medical monitoring includes both testing for early biological effect and an assessment of exposure using biological specimens (for example, blood or urine), when appropriate. This is provided as a service to individuals **in communities where there is believed to be an increased risk of disease from exposure to hazardous substances released into the environment** (p. 38841) (emphasis mine).

Nothing about this screening suggests that a monitoring agency/entity should take a given individual's personal medical history or other individualized considerations into account prior to implementing a medical monitoring program. Also, and importantly, ATSDR stresses the importance of confidentiality, a point overlooked by Dr. Guzelian, which would be contradicted by his unconventional approach. ATSDR states:

> Medical monitoring is one of ATSDR's service activities **and is not considered to be a research tool**.[8] The monitoring activity at each site will be routinely evaluated for the effectiveness of the screening tests in place and the types of effects being detected. **Due to confidentiality issues in dealing with small groups of people, the reporting from the system will consist of annual reports noting the number of individuals screened, the number of referrals made, and the number of conditions diagnosed in the referral system**. (p. 38843) (emphasis mine).

Dr. Guzelian's proclaimed need for consideration of individualized medical considerations and other factors is inconsistent with ATSDR's recommendations and contradictory to recommendations for confidentiality of medical records. This is contrasted by my proposed

[7] Federal Register Vol. 60, No. 145, Friday July 28, 1995: ATSDR's Final Criteria for Determining the Appropriateness of a Medical Monitoring Program Under CERCLA. Available at https://www.gpo.gov/fdsys/pkg/FR-1995-07-28/pdf/95-18578.pdf.

[8] I address Dr. Guzelian's mischaracterization of my proposed medical monitoring program as constituting "research" below.

medical monitoring program, which is consistent with ATSDR's recommendations and takes confidentiality seriously and into account.

Furthermore, those who have previously been involved with the implementation and/or administration of a medical monitoring program know from experience that insistence on consideration of individualized issues is not consistent with real-world experience. I have designed, led, or consulted on the creation, implementation, and ongoing administration of medical monitoring programs that have enrolled hundreds of thousands of participants of all ages for both work-related and broader environmental exposure reasons. In no case was advance consideration of individualized medical histories or other factors a criterion for inclusion, and in no case did a federal, state, industry/business, or other program partner request that consideration of such factors was needed or useful, and no program included any consideration of such factors. Instead, participants were included based upon a definition of exposure.

In fact, if the monitoring was for an employed individual who worked for a medical industry provider, who might otherwise therefore have the individual's personal medical records as well as the individual's medical monitoring records, then OSHA guidance and medical professional organization guidance provide that the standard of care is to keep the monitoring records separate from the patient's personal records. Consistent with ATSDR guidance, OSHA's guide to Medical Screening and Surveillance does not provide for any pre-review or consideration of personal medical histories or similar considerations for any of the exposure conditions which prompt monitoring.[9] In fact, such activity would require substantial ethical consideration under

[9] OSHA: Medical Screening and Surveillance Requirements in OSHA Standards, available at https://www.osha.gov/Publications/osha3162.pdf

OSHA guidance, which generally requires, for many reasons, that occupational health medical surveillance records not be mixed with personal medical records.[10]

Dr. Guzelian's arguments about the purported need to consider individualized differences and prior medical histories before implementing medical monitoring are further evidence of his unconventional views of risk assessment. Indeed, to the extent any individualized considerations, including medical histories, warrant consideration or attention after implementation of my proposed medical monitoring program, I have designed the program to accommodate such issues through various means, including the use of an initial survey questionnaire as well as through utilization of a Third-Party Administrator, whose program implementation and administration functions would include dealing with issues of eligibility of class members. Additionally, the proposed monitoring program is designed to send participants with an abnormal finding to that participant's personal health care provider for follow-up, and the personal provider is the right place and the right way to integrate the participant's individualized medical issues or other individualized factors into consideration – when and if that is necessary in the judgment of that provider. This is also fully consistent with ATSDR guidance for medical monitoring of community exposures.

2. My Comprehensive Literature Review and Analysis of the Epidemiologic, Toxicologic, and Physiologic Process Data was Equivalent to a Weight-of-Evidence Review Commonly Relied on by Experts in my Field.

Dr. Guzelian, while engaged in a review of the literature that dismisses findings from key epidemiological studies and completely ignores important recent studies conducted by governmental agencies, accuses me of failing to conduct a comprehensive literature review that

[10] United Stated Department of Labor, Occupational Safety and Health Administration. Clinicians. Available at https://www.osha.gov/dts/oom/clinicians/index.html#ethics

supports my opinion that members of the Bennington Exposure Class suffer from an increased risk of specific PFOA-related disease as a result of their above-background PFOA-exposures (Guzelian, at 13). However, as evidenced by my previous reports and the literature cited therein, I conducted a thorough and comprehensive literature search, informed and focused by years of expertise in identifying the most pertinent and persuasive studies. After identifying these studies, and based on an integration of the most consistent epidemiologic, toxicologic, and physiologic findings, I then selected disease outcomes/processes that were supported by the weight-of-evidence.

The weight-of-evidence approach not only values consistent findings in the epidemiologic literature, but also places them in context of what is known about toxicology and physiology. The focus of this approach is weight; it does not demand absolute consistency of epidemiologic findings for the simple reason that perfect consistency does not exist in nature, a point that Hill's criteria acknowledge. (Hill 1965; Ioannidis 2016). Thus, I did not "cherry-pick" from the literature or otherwise ignore pertinent epidemiological, toxicological, or physiological process evidence; instead, I appropriately emphasized and referenced the literature that represents the best synthesis of all of this information. As compared to Dr. Guzelian's methodology, which dismisses key studies and ignores other highly persuasive studies whose conclusions he doesn't agree with, I evaluated (and did not dismiss) the epidemiological, toxicological, and physiological literature for consistency of findings (or the absence of such consistency). My comprehensive literature review and analysis was thus consistent with and equivalent to the mainstream weight-of-evidence approach commonly relied on by experts in my field.

This strength of evidence methodology is recommended and utilized by federal agencies, including the ATSDR, and other experts genuinely concerned with understanding unifying

principles that explain otherwise seemingly diverse outcomes (Carbone et al. 2004). In fact, as demonstrated below, my PFOA-related disease outcome determinations were, in direct contrast to Dr. Guzelian's determinations, predictive of both dose-response and disease outcome findings contained in recent reviews conducted by state, federal, and international agencies. As a result, my determinations are aligned with both mainstream and emerging scientific consensus, as compared to the idiosyncratic opinions of Dr. Guzelian, which are based on a non-mainstream approach that has been characterized as more "aspirational" than realistic (Silbergeld and Scherer 2013).

I additionally rely on the opinions contained in Dr. Grandjean's expert rebuttal report as to the toxicity of PFOA, general causation, dose-response, and adverse health effects at individual endpoints resulting from exposure to PFOA.

Recent Agency Reviews

Governmental agencies and government supported organizations play an important role in developing scientific consensus regarding the effects of human exposure to the PFAS generally and PFOA specifically. In settings where dispute is inevitable and the credibility of opposing perspectives is in question, it is useful to consider the deliberations of reviewing agencies entrusted to interpret the evidence for public and policy purposes. This is particularly true as it is generally understood that the reviewers are experts and their deliberations and findings are created in the absence of vested interest. Indeed, due to the voluminous nature of relevant publications, active PFAS researches, like myself, rely on these reviews to assist in focusing on the key studies that are most persuasive for establishing thresholds, outcomes, or mechanisms.

Recent deliberations by US state, federal, and international bodies have addressed the issue of the contribution of PFOA contaminated drinking water to human exposures, as well as the

effects on human health following exposures. There is a strong correlation between the findings of these reviews and the health outcomes I have proposed to monitor for in Bennington. These reviews and their findings are thus further evidence of the reliability of my original literature search, as well as the unconventional (and outdated) opinions of defendant's experts.

Regarding exposure via contaminated drinking water, agencies, like the VTDOH,[11] have found consensus, i.e., that when drinking water is contaminated with PFOA, it becomes the predominant source of exposure in the affected population. As stated by the New Jersey Drinking Water Quality Institute (DWQI) in its report:

> It is well established that serum PFOA concentrations are greatly elevated in communities with highly contaminated drinking water resulting from environmental discharges (discussed in Biomonitoring, above). As discussed in Biomonitoring (above) and Toxicokinetics (below), continued exposure to even relatively lower drinking water concentrations which are more widespread (Section 3 above) can also substantially increase total human exposure, as indicated by serum PFOA levels.[12]

The recent agency reviews that have addressed water specifically (New Jersey, California, and ATSDR) substantially lowered the recommended threshold for the safe (versus unsafe) exposure to the toxic PFOA. The thresholds are in the range of 10-15 ppt in water, and ingestion of drinking water contaminated at this level over time will result in internal human contamination of around 1-2 µg/l in humans consuming the water at steady state. Not surprisingly, this is also the range of internal contamination level at which dose-response adverse effects can be seen in humans with internal contamination and animals in toxicology studies. It is a health-based level, and not random or coincidental. It was chosen as a threshold for us in this case, as it was by these

[11] As addressed in my first expert report, the VTDOH found that blood serum PFOA levels of Bennington residents were strongly correlated with PFOA levels in drinking water, i.e., that consumption of contaminated drinking water was the primary source of PFOA exposure.

[12] New Jersey Drinking Water Quality Institute, Health Effects Subcommittee: Health-Based Maximum Contaminant Level Support Document: Perfluorooctanoic Acid (PFOA), at 41 (June 27, 2016).

responsible agencies, based on the weight-of-evidence concerning thresholds of response in the most persuasive studies.

The NJ DWQI also concluded that the mean steady state drinking water-to-serum contamination level bio-concentrated PFOA levels 100-fold.[13] A rough calculation from this conclusion is that the average person, ingesting PFOA-contaminated water at 14 ppt (the New Jersey threshold), over a period of time will have 1.4 ppb PFOA in their serum, a figure that may be recorded as 1 ng/ml or alternatively as 1 μ/L.

In regard to disease outcomes, both ATSDR and EFSA took a "weight of evidence" approach, as I did, while New Jersey took a more formal "risk assessment" approach, which California relied on (as well as other reviews). The table below reviews the conclusions of ATSDR, New Jersey and California, and also those of an international body (European Food Safety Authority ("EFSA")), for the health outcomes I selected for medical monitoring by clinical laboratory testing or other protocols (home blood pressure monitoring). Table 1, below, demonstrates health outcomes of PFOA exposure regardless of source, as ATSDR, New Jersey, and California were considering contaminated water, whereas the EFSA considered contaminated food.

[13] Id. at 50.

TABLE 1: Conclusions of Recent Reviews for Proposed Monitoring Disease Outcomes

Outcome	Review Agency			
	ATSDR[14]	NJ DWQI [a 15]	Cal St WQCB [c 16]	EFSA Contam[17]
Liver Damage	+	+	+	+[d] ("strong support")
Increased serum lipids (Cholesterol and LDL Cholesterol)	+	+[b]	+	+ ("strong support")
Pregnancy Induced Hypertension	+	+		
Thyroid Disease/Effects	+		+	insufficient
Uric Acid[f]		+		insufficient
Cancer				insufficient[e]
Kidney Cancer		+	+	
Testicular Cancer		+	+	
Presence in Breast Milk[g]	+	+	+	

a The NJ Drinking Water Quality Institute (DWQI) considered the human data but used animal rather than human endpoints to derive its Maximum Contaminant Level (MCL) recommendations. The NJ DWQI cited both human and animal data for its conclusions regarding liver and lipid toxicity and noted that MCLs were in a similar range for either consideration. For the mechanisms of liver effects, the NJ DWQI, ATSDR and EFSA cited both PPAR and non-PPAR mechanisms. As stated by EFSA: "Liver lesions occurred in all three animal models, with occurrence in PPARa knockout animals thereby pointing to the fact that these lesions occur independent of PPARa (Filgo et al., 2015)" (p. 90).

b The NJ DWQI noted that five of the then 20 available lipid studies had designs that were not cross-sectional, including two longitudinal studies which also found the relationship (p. 75).

c The California Division of Drinking Water Resources Control Board made its recommendations after reviewing the deliberations of the Office of Environmental Health Hazard Assessment (OEHHA).

d EFSA noted the liver is also a target organ in rodents. And, it indicated that the causal association is an "adverse" effect (p. 177). EFSA regarded disrupted cholesterol metabolism as the critical effect. It notes that increments in serum dose above 25ng/ml does not appear to further increase the risk (p.171, meaning: the dose-response curve flattens out, or plateaus).

e Regarding cancer, EFSA stated that its review agreed with the International Agency for Research on Cancer (IARC) that PFOA should be classified as Group 2B ("possibly carcinogenic to humans") (p. 131).

f ATSDR noted that the epidemiologic literature shows consistent association of PFOA to hyperuricemia, but it did not reach any other discernible conclusion.

g Presence in breast milk and concern about timing of pregnancy related to serum contamination are recommended for educational programs only, so that affected individuals have access to an interested and expert resource.

[14] ATSDR: Toxicological Profile for Perfluoroalkyls, available at https://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=1117&tid=237

[15] New Jersey Drinking Water Quality Institute, Health Effects Subcommittee: Health-Based Maximum Contaminant Level Support Document: Perfluorooctanoic Acid (PFOA) (June 27, 2016).

[16] California State Water Quality Control Board: Perfluorooctanoic acid (PFOA) and Perfluorooctanoic Sulfonate (PFOS), available at https://www.waterboards.ca.gov/drinking_water /certlic/drinkingwater/PFOA_PFOS.html

[17] EFSA CONTAM Panel, Scientific Opinion on Risk to Human Health of PFOS and PFOA in Food, EFSA Journal 2018; 16(5):5194, doi:10.2903/j.efsa.2018.5194.

In reaching their conclusions, the human health outcomes were not the only topic considered by these reviewing bodies. ATSDR, EFSA, and New Jersey also considered both animal and cell physiologic data. The conclusions concerning animal data are quoted because they are responsive to the same weight-of-evidence approach (which considers and does not dismiss pertinent evidence) that I took in previous reports, seeking corroboration of human findings or the absence of corroboration in toxicological evidence. As provided in the New Jersey report:

> Hepatocellular hypertrophy is a consistently reported histopathological finding for PFOA that accompanies increased absolute and relative liver weight. A number of studies in both nonhuman primates and rodents also report other **histopathological changes** that are indicative of **liver injury** and/**or lipid accumulation in the liver**. These effects occurred at doses similar to those causing increased liver weight. Notably, prenatal exposure to a very low dose (0.01 mg/kg/day) of PFOA caused liver toxicity that persisted until adulthood at doses below those which caused increased liver weight (Quist et al., 2015).[18] The liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were increased in all dose groups (> 0.49 mg/kg/day) in a study of mice dosed with PFOA in drinking water for 21 days (Table 8). These increases were statistically significant (p2.64 mg/kg/day for AST and >17.62 mg/kg/day for ALT (Son et al., 2008) (emphasis added).[19]

ATSDR compared serum lipid concentrations to serum PFOA concentrations (p. 171-76). ATSDR (p. 11, p 185) and EFSA (pp. 193-4) also discussed experimental evidence showing non-PPAR mechanisms of liver damage and of steatosis (fatty infiltration of cells) in test animals, a topic which tracks the initial insult (disrupted sterol metabolism) to two outcomes which are present in humans, elevated total and LDL cholesterol, and liver toxicity. Note that, while Dr. Guzelian insists on focusing on only one mechanism of injury, there is agreement that more than one mechanism of injury is at work, and some have been characterized. The agencies noted that PFOA causes disrupted cholesterol metabolism and that this has led to higher cholesterol in humans, as well as liver toxicity, and both ATSDR and EFSA pointed out that we understand some but not yet all of the reasons this occurs.

[18] New Jersey Drinking Water Quality Institute, Health Effects Subcommittee: Health-Based Maximum Contaminant Level Support Document: Perfluorooctanoic Acid (PFOA) (June 27, 2016) at 111 (emphasis mine).
[19] Id., at 116.

The animal and in vitro findings referenced in my previous reports and discussed in these agency reviews are a normal part of scientific corroboration under Hill's "criteria"[20] (Hill 1965) and also consistent with Ioannidis' modern commentary about how we consider Hill's criteria five decades later (Ioannidis 2016). The experimental animal data and cell physiologic data add to the human data and are further responsive to topics such as "biological plausibility," "coherence," and "experiment," the areas where we normally seek outside confirmation (or absence thereof) of the existence of explanatory and unifying mechanistic information in other species or cell systems. The concept of lipid accumulation in the liver of animals is called steatosis when it occurs in humans, and steatosis is the initial (and potentially reversible) stage of NAFLD. A critic determined to ignore and dismiss evidence can, and has, characterized outcomes as diverse and inexplicable. However, my review and subsequent agency deliberations point to underlying mechanistic findings that explain outcomes, which is a conventional scientific when considering causation. A full reading of Hill's criteria and of Ioannidis' subsequent and modern review reveal that there is agreed upon acknowledgment that health outcomes of toxic exposures are rarely "specific" to a single disease or organ, (Hill 1965; Ioannidis 2016), and Ioannidis further points out that the most rigorous test of epidemiologic findings is comparison to the experimental literature. This was considered both in my weight-of-evidence review and in the reviews of these agencies.

In differing ways based on the approach they took, ATSDR and New Jersey also considered susceptible populations, i.e., subgroups whose health effects may occur when similar health effects are not noted in the entire population. These populations mentioned by ATSDR are of particular pertinence to the consideration of medical monitoring of the Bennington Exposure Class: children,

[20] As noted by Dr. Grandjean, Hill's criteria are more appropriate referred to as "aspects," as he did not intend them to be a checklist of causal criteria as Dr. Guzelian has employed them in this matter. Grandjean rebuttal report, at 25.

and populations more highly exposed, i.e., above-background, as compared to the general population. Several health outcomes associated with PFOA exposure were also mentioned in regard to susceptible populations, including cholesterol (in children), and uric acid in those who also have hypertension. (ATSDR, pp. 515-518).

In summary, there is support in these recent reviews for each of the disease outcomes selected for inclusion (and followed by directed laboratory testing or clinical testing such as in-home blood pressure monitoring in pregnant participants) in my recommended medical monitoring program. As is normal when the underlying science is epidemiology, (Hill 1965; Ioannidis 2016), the agreement among review groups is not perfect for all topics. However, there is a substantial clarity that these agencies reviewed the same literature that I reviewed, and the findings of these agencies demonstrates that the same human population evidence and animal toxicology and cell physiology literature was considered.

B. Dr. Guzelian's Mischaracterizations of the Bennington Medical Monitoring Program.

Dr. Guzelian mischaracterizes multiple aspects of my proposed Bennington medical monitoring program as described in detail in my merits report of December 15, 2017. I will briefly respond to these mischaracterizations here, which appear to me as repetitive, confusing, and unhelpful attempts to confuse matters for the Court.

First, Dr. Guzelian's mischaracterizes my proposed monitoring program as "research" in a completely unsupported statement (Guzelian, at 11). Nowhere in either of my previous two expert reports is any research component of the proposed medical monitoring program proposed or listed, and there is no "cost" for any research component contained in in the expert report(s) of Donald R. Brandt with CTI Administrators, Inc. I have participated in epidemiologic research regarding PFAS, and I do believe in the additional public benefit that a research arm can bring to a medical

monitoring program. However, there is simply no such component to my proposed Bennington monitoring program.

Second, Dr. Guzelian misstates the purpose of my proposed use of a survey questionnaire as part of my monitoring program (Guzelian, at 12). As is clear from my previous reports, Dr. Guzelian's assertion that the survey is a "search" tool to locate individuals for inclusion in my monitoring program is simply false. Rather, the survey will be used for the purposes described in my previous reports, i.e., to collect valuable information from participating class members prior to, and then continuing throughout the life of, the program in order to most effectively monitor and evaluate this exposed population. This is consistent with previous, yet frankly less targeted predecessor medical monitoring efforts whose survey methods have been described in the medical monitoring peer-review literature (Wones et al. 2009). However, the proposed Bennington survey is far more targeted and discrete than peer-described predecessor activity as the proposed Bennington biomonitoring activity and associated survey detects new conditions for referral to treating clinicians in those who already qualify for participation; however, it does not (and cannot) identify participants because they are identified by their exposure.

Importantly, the survey will also serve to obviate the need for any consideration of the extremely unconventional and problematic contention of Dr. Guzelian as to the purported need to consider individualized factors and personal medical histories prior to implementation of the monitoring program. Dr. Guzelian's suggestion for consideration of such individualized issues is completely inconsistent with the medical literature, whereas the survey is the conventional way to address diagnostic and symptomatic reports of individual participants. Finally, in order to correct an impression left by Dr. Guzelian's report, I again note that while the survey will be modeled after the existing C8 Health Survey, the C8 survey is not the intended final product for use in my

proposed Bennington program. To the extent the C8 survey contains components that are not relevant to the proposed Bennington monitoring program, such components would not be used, and likewise any missing components necessary for the proposed Bennington program will be added.

Third, Dr. Guzelian conflates the requirement of demonstrating "above-background" levels of PFOA through a blood test in order to be eligible for medical monitoring as part of the Exposure Class with the ongoing PFAS blood serum testing, which is part of my proposed monitoring program (Guzelian, at 13). In terms of program eligibility, the "above-background" selected biomarker of internal contamination serves as well-documented proof of human internal contamination, and this initial test provides for exclusion when such proof is absent. This is a higher standard for proof of eligibility than the mere assumption that opportunity for contact with delivered, contaminated water would necessarily lead to internal contamination.[21]

In contrast to the use of a PFOA blood serum test as an initial and rigorous inclusion/exclusion criteria for class members, the inclusion of ongoing PFAS blood serum testing in the monitoring program protocol is essential for the well-being of validated, accepted program participants. This is so participants can verify that their internal PFOA contamination is declining over time, as opposed to merely assuming that it is declining, due to cessation of consumption of contaminated drinking water. It thus addresses the health needs of the community to verify that the source of exposure has been addressed, and also the emotional well-being of individual participating class members. The ongoing PFAS testing is also important to ensuring proper

[21] Indeed, the actual demonstration of internal contamination is also a higher than the standard of proof that ATSDR demands of its own efforts.

ongoing administration of the proposed program, including addressing potential additional areas of concern such as breast-feeding of newborns.

Fourth, Dr. Guzelian repeatedly references purported "differences" between my first and second expert reports (Guzelian, at 14-16), ostensibly to show some flaw in my reasoning or error in my judgment. However, any "differences" between the two reports simply demonstrates the deliberative process I undertook in formulating my opinions in this matter. My first report discussed disease outcomes and processes associated with exposure to PFAS generally and PFOA specifically, and my second report considered these outcomes and processes in terms of suitability for my proposed medical monitoring program. The consideration of each disease outcome included, but was not limited to, four components: (1) the presence of a causal condition; (2) the availability and suitability of useful, clinically recognized testing (or, in the case of ulcerative colitis, survey symptoms) that is diagnostic of, and will lead to earlier detection of, the disease outcome/condition; (3) consideration of any countervailing presence of potential harms that could result from the testing; and (4) a consideration of whether the testing would be duplicative of what members of the Exposure Class would otherwise receive should that individual seek regular medical care.[22] I will discuss the test considerations in more detail in a subsequent section of this report.

Fifth, Dr. Guzelian repeatedly asserts that I gave no consideration to potential "harm" in the design of my proposed medical monitoring program testing protocols (Guzelian, at 12). However, I did in fact consider the balance of benefits and harm when selecting the specific disease

[22] These components are consistent with authoritative guidance concerning the basis for medical monitoring for environmentally induced conditions. ATSDR: Final Criteria for Determining the Appropriateness of a Medical Monitoring Program Under CERCLA. FR Vol 60. No. 145, Friday, July 28, 1995. Available at https://www.gpo.gov/fdsys/pkg/FR-1995-07-28/pdf/95-18578.pdf

outcomes and diagnostic clinical tests for inclusion in the proposed monitoring program. As evidenced by the deliberative process between my first and second reports, I considered a broad array of disease outcomes related to PFOA exposure, but only recommended specific disease outcomes (ones most amenable to early detection and practical intervention) for inclusion in my proposed program, in part due to considerations of "harm." Similarly, I considered a number of diagnostic clinical tests, but only chose certain ones, again in large part due to considerations of "harm," directly from the testing (such as outpatient venipuncture, which ATSDR considers and defines as not hazardous) as well as the implications of false positives, false negatives, or any related ambiguities pertaining to follow-up. Thus, as I testified to during my deposition, I did in fact consider "harm" as well as benefits when deliberating over the components of my monitoring program, and the repeated assertions otherwise belong to Dr. Guzelian alone.

Finally, Dr. Guzelian has consistently applied an unconventional and misleading context to the word "asymptomatic." The word "asymptomatic" as applied to medical monitoring does not mean that participants are required to be symptom-free, as such an expectation as a criterion for participation is not compatible with the human condition or with OSHA and ATSDR directives for medical monitoring. Federal agencies do not recommend elimination of participants from monitoring programs who have a symptom, nor do I in my proposed Bennington monitoring program. The failure by Dr. Guzelian to clarify that "asymptomatic" does not mean symptom-free is also not compatible with my extensive experience in implementing and administering medical monitoring programs, as disqualifying participants at the first appearance of symptoms is not how monitoring is conducted in a real-world setting. Instead, "asymptomatic" means that the medical monitoring program detects disease before the program participant would otherwise obtain a diagnosis (for an environmental-caused condition).

Stated differently, the word "asymptomatic" is intended to distinguish only those participants in the program from those whose disease symptoms would already have led to a formal, causal, diagnosis.[23] Clinicians know that few people are symptom-free, and the mere presence of symptoms cannot be equated with completed diagnoses or completed diagnoses leading to useful interventions. Furthermore, in most medical monitoring programs, the finding of one known outcome does not preclude the continued monitoring for characterization of disease status for the presence or absence of disease progression; that is one of the points of workplace hearing testing under OSHA, for example. And, in no case does the presence of one disease caused by exposure preclude the ongoing search for others considered to be caused by the exposure.

C. The Proposed Bennington Medical Monitoring Program Will Result in Early Detection of PFOA-Related Disease Outcomes as Compared to What Would Otherwise Occur Through Regular Medical Care and will Result in Substantial Benefits to the Exposed Population.

Dr. Guzelian, again applying his unconventional criteria for medical monitoring - which would require potentially years of additional studies and expectations of unrealistic evidence in order to justify medical monitoring, while exposed class members missed out on the chance to have adverse health outcomes detected early - contends that my proposed monitoring protocol for the Bennington Exposure Class will not result in the early detection of disease, and further will not be effective or beneficial to the Bennington Exposure Class (Guzelian, at 119). He also, in an illogical, contradictory assertion, argues that the proposed testing, which he contends will not lead to early detection of disease, will somehow duplicate routine preventive care already received by class members through their primary physicians (Guzelian, at 122).

[23] This same rationale applies to Dr. Guzelian's arguments about the "eligibility" of the named plaintiffs for medical monitoring based off of their medical histories.

As discussed in my second expert report and above, based on my clinical expertise and extensive knowledge of PFAS, and considering a number of factors, I selected specific PFOA-related disease outcomes that are amenable to early detection for inclusion in my proposed Bennington medical monitoring program. Furthermore, I recommended a comprehensive diagnostic monitoring protocol, consisting primarily of clinical laboratory tests, which will be useful in the early detection of each these disease outcomes and which are not duplicative of medical care otherwise received by class members who regularly seek preventive medical care. For these reasons, the proposed Bennington medical monitoring program will result in substantial benefits to not only participating class members, but the Bennington community as a whole.

1. <u>The Recommended Monitoring Protocol Will Lead to Early Detection of Disease and Improve Health Outcomes</u>.

A fundamental tenant of clinical medicine is that the earlier we can detect a disease, the better the health outcome will likely be for the patient. Many, but not all, of the adverse health outcomes associated with PFOA exposure are amenable to a biomonitoring program designed to improve human health through early detection. Therefore, in selecting specific disease endpoints for inclusion in the proposed Bennington medical monitoring program, I undertook a deliberative process to select the outcomes that are most amenable to early detection, including consideration of the factors discussed above (causality, useful testing, harms, potential for duplication), as well as ATSDR guidance, which provides:

> **<u>Outcome Criteria</u>**
>
> B. **The monitoring should be directed at detecting adverse health effects that are consistent with the existing body of knowledge and amenable to prevention or intervention measures** …. In addition, ***the adverse health effects (disease process, illness, or biomarkers of effect)***[24] should be such that early

[24] Dr. Guzelian's critique ignores the critical point that ATSDR considers "biomarkers of effect" are considered as useful outcomes of medical monitoring (Guzelian, at 34).

> detection and treatment or intervention **interrupts the progress to symptomatic disease, improves the prognosis of the disease, improves the quality of life of the individual, or is amenable to primary prevention** …. An easily detectable effect is one that can be found on clinical examination, or through the use of simple, diagnostic tests in an outpatient setting. (p. 38841, emphasis mine).

Based on the foregoing, as well as my expertise in PFAS and my clinical experience and expertise, I selected the following specific PFOA-related disease outcomes/processes to monitor for in the Bennington Exposure Class:

- Kidney Cancer
- Testicular Cancer
- Pregnancy-Related Conditions
    - Pregnancy-Induced Hypertension
    - Thyroid Disease (Pregnancy)
    - Shortened Duration of Breastfeeding
- Thyroid Disease
- Liver Function Abnormalities/NAFLD
- Hyperlipidemia
- Ulcerative Colitis
- Uric Acid Abnormalities and Gout

These diseases meet ATSDR outcome criteria as well the other criteria referenced above as they are amenable to early detection, because treatment and intervention can interrupt the progress to symptomatic disease, and because they are "easily detectable" effects.

In choosing the specific laboratory/clinical tests to include in the monitoring protocol, I reviewed applicable screening guidelines, including those of the USPSTF and other professional medical organizations, relied on my many years of clinical experience, and considered pertinent ATSDR guidance, which specifies that (1) the test is directed at a diagnostic condition which is caused by the exposure; 2) the test can lead to earlier detection of the targeted disease; 3) the earlier detection can lead to successful intervention that can reverse, or delay, or mitigate the

progression of disease; and 4) the test is routinely available in the participant's community, familiar to participants' health care providers, and providers will understand the test and its follow-up;[25] and 5) the benefits of testing outweigh the harms. A way to summarize this ATSDR process is that the tests must be directly useful to the participants and/or their treating clinicians, as it is the treating clinicians, and not the medical monitoring program physician, who receive referrals and follow up on testing as needed and make any clinical diagnoses.

Taking into account the foregoing, as well the Exposure Class members' increased risk of disease, I chose a clinical monitoring protocol that will be useful in the early detection of these disease outcomes and improve overall health outcomes. The clinical tests chosen can lead to earlier definitive diagnosis and each is used routinely in the community for that purpose. For example, ATSDR is clear that venipuncture (the drawing of a tube of blood for testing purposes) is regarded as noninvasive and acceptable by ATSDR in its guidance. However, what is different in the proposed monitoring program, as discussed in more detail below, is to introduce the testing at the asymptomatic phase, which is consistent with the goal of earlier detection. Of course, each disease detected at an earlier stage has a better prognosis and a greater chance of full reversal or mitigation, and will thus be of substantial benefit to the Bennington community as a whole.

Dr. Guzelian attempts to make the case that the proposed testing will not lead to early detection of disease, contending that the clinical tests are either not diagnostic of the disease outcomes, or that they will be duplicative of preventive care already received. However, as discussed below, Dr. Guzelian's critiques don't stand up to scrutiny, as the tests will in fact lead to early detection through either being diagnostic or through the referral aspect of the monitoring

[25] I also gave consideration to how local clinicians in Bennington would react to my proposed protocol, as some of these medical professionals will be involved in implementing the monitoring program on the ground (and/or be the recipients of referrals out of the program) and thus it is important that they are comfortable with the protocol.

program. The statistical principles include a high enough predictive value of these tests to be clinically useful in disease detection, and, in the time frame of the disease when prevention or mitigation is still possible. In addition, the tests chosen represent the current standard-of-care for noninvasive testing, in keeping with ATSDR guidance. This point is further illustrated by the fact that these clinical tests are all targeted to specific International Classification of Disease ("ICD") codeable diagnoses, and, specifically, the 10th edition, known as the ICD-10. These ICD-10 codes are described as "clinical" in their intent,[26] and are specifically intended for description of medical encounters "in all settings."[27] Ex. A contains a chart of the proposed monitoring program testing correlated with the ICD-10 codes pertinent to the proposed Bennington medical monitoring program.

Thyroid Disease

Dr. Guzelian's contends that the USPSTF does not recommend screening in asymptomatic adults for thyroid dysfunction, and gave thyroid screening an "I" grade (Guzelian, at 84). The primary screening test used for the detection of thyroid dysfunction is the thyroid stimulating hormone or TSH with a sensitivity and specificity of well over 90%. Predictive values are influenced by population prevalence, which is between 3-5% in the general population (Hollowell et al. 2002). Screening is not recommended for the general population by the USPSTF, in the absence of risk factors. However, the exposed Bennington population constitutes an at-risk population, and, the USPSTF has emphasized that the risks of undetected disease are substantial with a significant preventable morbidity. Competent clinicians are able to choose patients who need close watching and select for treatment those who actually need an intervention.

[26] Preface to ICD-10-CM. Available at https://www.cdc.gov/nchs/data/icd/FY2018_Preface.pdf
[27] ICD-10-CM Official Guidelines for Coding and Reporting FY 2018 (October 1, 2017 - September 30, 2018) Available at https://www.cdc.gov/nchs/data/icd/10cmguidelines_fy2018_final.pdf.

Thus, in response to Dr. Guzelian, I first note that he has failed to address the increased risk of disease present in the Bennington Exposure Class in his critique, which is clinically inappropriate. Regarding the "I" grade, this means only that USPSTF has not found sufficient evidence to make a recommendation for or against medical monitoring in the general population, which is different than indicating that the harms outweigh the benefits. In a high-risk population, the proposed medical monitoring program meets ATSDR recommendations and is no way contradictory to USPSTF deliberations. Dr. Guzelian further selectively cites from the American Thyroid Association, (Guzelian, at 85), and, based on no evidence, assumes that any etiology not listed in his selected citation is considered and rejected. That is either deliberately misleading or, in the best case, just an absurd assumption. Nothing about these guidelines implies that they have considered PFOA or are even aware of the deliberation of environmental agencies like those already reviewed in this report. In fact, these same ATA guidelines go on to say that:

> … more frequent screening may be appropriate in high-risk or symptomatic individuals." (Garber et al. 2012) (emphasis mine).

Dr. Guzelian omitted this statement, i.e., "cherry-picked." I have shown that PFOA- exposed individuals are at an increased risk for thyroid disease, and the "bottom line" is that more frequent screening is recommended for risk populations, and therefore my screening recommendation is clinically appropriate and supported by testing with strong statistical performance parameters.

Pregnancy-Induced Hypertension

Dr. Guzelian attempts to discredit my recommendation for blood-pressure monitoring pertaining to Pregnancy-induced Hypertension based on his assertion that "regular prenatal care already includes blood pressure monitoring" (Guzelian, at 92). Gestational hypertension (Pregnancy-induced Hypertension or PIH) is characterized by new-onset elevations of blood pressure (BP) after 20 weeks of fetal gestation. (American College of Obstetricians and

Gynecologists, or ACOG, 2013).[28] High blood pressure during pregnancy can lead to significant morbidity and mortality for the mother and baby due to its potential for causing complications (Buchbinder et al. 2002). In mothers with PIH there is a risk of progression to preeclampsia (the most serious of the potential complications from PIH) of around 25% and thus women with gestational hypertension require close monitoring throughout pregnancy (Tranquilli et al. 2014).

Because of this increased risk of complications in women with PIH, the American College of Obstetricians and Gynecologists (ACOG) states that women with PIH "require enhanced surveillance of blood pressure," beyond what would normally be offered in an uncomplicated pregnancy. Specifically, ACOG recommends that women with gestational hypertension undergo blood pressure monitoring at least once weekly, with an additional weekly measurement at home (ACOG 2013). Thus, the medical monitoring program, as it pertains to PFOA-exposed women, must insure that the recommended "enhanced surveillance" of blood pressure will begin in a timely manner and that the women's increased risk for PIH/preeclampsia is conveyed to the treating obstetrician or family physician. This recommendation is clinically appropriate, and, the home monitoring provides the earliest chance for detection and does not rely on the happenstance of a clinical visit.

Thyroid Disease in Pregnancy

Dr. Guzelian asserts that screening for thyroid disease during pregnancy is a controversial topic, (Guzelian, at 92); however, his statement is clinically misleading. As stated by in an evidence-based review from the American Academy of Family Physicians:[29]

[28] ACOG. Preeclampsia and Hypertension in Pregnancy: Resource Overview. Available at https://www.acog.org/Womens-Health/Preeclampsia-and-Hypertension-in-Pregnancy and https://www.acog.org/~/media/Task%20Force%20and%20Work%20Group%20Reports/public/HypertensioninPregnancy.pdf.

[29] American Academy of Family Physicians. Thyroid Disease in Pregnancy. https://www.aafp.org/afp/2014/0215/p273.html

> Thyroid disease is the second most common endocrine disorder affecting women of reproductive age, and when untreated during pregnancy is associated with an increased risk of miscarriage, placental abruption, hypertensive disorders, and growth restriction. Current guidelines recommend targeted screening of women at high risk, including those with a history of thyroid disease, type 1 diabetes mellitus, or other autoimmune disease; current or past use of thyroid therapy; or a family history of autoimmune thyroid disease. Appropriate management results in improved outcomes, demonstrating the importance of proper diagnosis and treatment**. (Carney et al. 2014)** (emphasis mine).

Clearly, appropriate management of thyroid disease during pregnancy is critical to a variety of health outcomes, and thus it is difficult to imagine how screening in an at-risk population could be controversial. Further, Dr. Guzelian has also already noted that the American Thyroid Association ("ATA") has not explicitly included PFOA on their list of causes of thyroid disease (as to imply this means that the ATA has actually reviewed the recent evidence and found it wanting). The ATA and ACOG both recommend monitoring for pregnant women if there is increased risk of thyroid disease. As a result, I have recommended monitoring of the exposed Bennington population who are at an increased risk of thyroid disease, and this recommendation is clinically appropriate.

Hyperlipidemia

It is generally accepted that screening for hyperlipidemia is inherently valuable for prevention of disease. In terms of test performance, the laboratory test defines the condition, and is highly repeatable. More than 95% of individuals who screen positive for hyperlipidemia under normal testing conditions will have the disease. Dr. Guzelian's concern is not with the efficacy of the test, but with the concept that the testing will be duplicative, i.e., obtained in during regular preventive care. While there may be potential for overlap applicable to the general population, that overlap will not be absolute nor even nearly so, as the initiation of testing is earlier in the proposed monitoring program, and the frequency is greater, as compared to the recommendations applicable to the general population. Thus, again, this screening recommendation is clinically

appropriate.

Kidney Cancer

In regards to kidney cancer screening, Dr. Guzelian again takes a concept out of its proper context and uses his new context to support his argument. While he is correct that an urinalysis cannot, in and of itself, make a complete diagnosis of kidney cancer (Guzelian, at 90), he is misleading and incorrect because, as set out in my second report, the urinalysis is a screening test that is reviewed by the program physician who then refers a participating class member to their primary care clinician for follow-up testing and diagnosis. Thus, the combination of hematuria and follow-up does a fine job of algorithmic screening. Further, while the urinalysis alone is neither sensitive nor specific, it will detect abnormalities, and, if they are consistently present at follow-up, the follow-up testing is highly likely to detect disease if present and to confirm the need for intervention.

Regarding Dr. Guzelian's reference to my deposition answer, there is no test short of renal biopsy with examination of histopathology that definitively diagnoses kidney cancer. The same logic that Dr. Guzelian has applied to urinalysis in the case of kidney cancer could also dismiss mammography which does not "diagnose" breast cancer, or Human Papilloma Virus ("HPV") screening because it only detects risk factor(s) for cervical cancer and does not "diagnose" the disease. Guzelian's critique thus deliberately conflates the desirability of screening with the subsequent need to obtain a definitive diagnosis when screening indicates. For all of the foregoing reasons, my recommendation for screening is clinically appropriate.

Gout and uric acid

Dr. Guzelian contends that there is insufficient evidence to demonstrate that reducing uric acid levels in "asymptomatic" patients provides a treatment benefit (Guzelian, at 87). However, there are two major problems with Dr. Guzelian's critique. Frist, elevated uric acid is an important

clinical marker for more than just gout and renal or ureteral nephrolithiasis. It is also biomarker of effect, which means it is proper to monitor for or track under ATSDR guidance. Second, uric acid is also (and importantly) an independent risk factor for other diseases, and studies that have controlled for multiple risk factors find that gout is an independent risk factor for the development of hypertension in adults and children, (Alper et al. 2005; Forman et al. 2007; Mellen et al. 2006; Nagahama et al. 2004), for metabolic and cardiovascular disease, (Feig et al. 2008a; Niskanen et al. 2006), (Niskanen et al. 2004), and (Alderman et al. 1999) and for renal disease, (Feig et al. 2008b; Iseki et al. 2004; Niskanen et al. 2004).

Dr. Guzelian further makes the mistake of assuming that the only logical intervention is a medical treatment. If the only available intervention for early-detected disease were pharmaceutical, he would have a point because pharmaceutical intervention is generally reserved for clinically apparent disease. Pharmaceutical treatment can be necessary, but the logical initial intervention following a medical monitoring detection of the early condition is a lifestyle intervention. This is a beneficial step and without risk of harm, it can be taken at an early stage in disease process, and the hyperuricemia validates the step under ATSDR guidance and also provides a motivating factor for the personal implementation of lifestyle change when the desirability of lifestyle change is presented by the participant's own clinical provider. For these reasons, my screening recommendation pertaining to uric acid and gout is clinically appropriate.

Liver Function Testing

Dr. Guzelian critiques the proposed liver function tests on statistical grounds and for a purported absence of evidence that these tests can lead to improved care and better outcomes (Guzelian, at 62). As is clear, the conditions sought are fatty change of liver, steatosis, or more severe forms of the same processes that also feature inflammation, including steatohepatitis.

Laboratory abnormal liver function tests are not that sensitive for the initial and early stage of NAFLD called steatosis, or fatty change in the liver. However, the idea that these are sharp cut-offs is incorrect, and clinicians use their judgment in selecting patients for further evaluation when liver function tests show patterns suggesting possible disease. Trends including elevating test results over time in an at-risk participant can be reasons that a clinician investigates further. And, the test deficiency is that it is insensitive, and thus individuals who have clearly abnormal tests are near certain to have liver disease.

Further, the use of liver function tests which are repeatedly abnormal in human studies of PFOA-exposed populations is highly consistent with the already quoted ATSDR guidance that biomarkers of harmful outcomes are useful. Most importantly, clinicians can and do combine the screening liver function tests with algorithms of other readily available and noninvasive testing to detect patients/participants who have early signs of disease and are at highest risk of progression. Here is what the British Medical Journal Best Practice website says about the proposed tests in the setting of risk of hepatic steatosis.

> 1st investigations to order:
>
> - serum AST and ALT
> - total bilirubin
> - alkaline phosphatase
> - gamma glutamyl transferase[30]

These tests are aimed at detection of a condition which is present at baseline in at least 20-30% of the population. For such a prevalent and clinically important condition, clinicians have cause to be on the lookout for the need to initiate an evaluation for the early and silent disease. And, the liver disease risk is known to be increased in the presence of elevated PFOA contamination – all reviewing authorities agree on this point. The reason that monitoring is valuable is that, most

[30] BMJ Best Practice. Hepatic Steatosis. Available at https://bestpractice.bmj.com/topics/en-us/796

often, asymptomatic early disease will progress to more serious disease in at least 10% of these people with the incipient, early disease process.

The British Medical Journal and the British National Institute for Health and Care Excellence ("NICE") have offered the following about how non-alcoholic fatty liver disease (NAFLD) is generally diagnosed:

> NAFLD is usually diagnosed in primary care incidentally either by abnormal liver blood tests or an abnormal liver ultrasound appearance picked up as part of an investigation for an unrelated condition.[31]

I note that the NICE guidelines are clear that one of the benefits of earlier diagnosis is the opportunity for management by "non-pharmacologic treatment (for example: diet and exercise)." I am proposing to make the incidental detection of a common and important disease process into planned detection in a high risk population. That does not mean that all disease will be detected, but it does mean that more disease will be detected and earlier interventions will be possible. Of course, again, it does not mean that liver function tests in the proposed monitoring program stand alone. Rather, when the results of such tests are abnormal or suspicious, they will be followed by other testing. My recommendation for screening for liver function testing is clinically appropriate.

2. The Recommended Diagnostic Monitoring Protocols are Different from what Class Members Would Otherwise Receive in the Course of Regular Preventive Care.

Dr. Guzelian further presents a paradoxical assertion -- that the proposed monitoring program, which he criticizes for lack of efficacy -- also duplicates routine preventive care aimed at recognized standards of early detection that will be received anyway. No reliable information is provided to back up this assertion, as the review of a handful of medical records for potential

[31] National Institute for Health and Care Excellence (NICE, Great Britain). Non-alcoholic fatty liver disease: assessment and management. Available at https://www.ncbi.nlm.nih.gov/books/NBK384717/?report=reader

duplication is very different from Dr. Guzelian's otherwise strong respect for statistical design. More importantly, the data he provides actually support the opposite case, as the records referenced are in concerned patients who sought specific care and who received only sporadic and inconsistent elements of the proposed program.[32] Thus, the proposed monitoring program and its proposed clinical testing protocol fills a gap in the needs of a small but coherent exposure community with a specific list of excess risks that will benefit from medical monitoring. For these reasons, and the reasons discussed below, the diagnostic monitoring protocols in my proposed medical monitoring program for the Bennington Exposure Class is not duplicative of otherwise recommended care.

As members of the Bennington Exposure Class have all been exposed to above-background levels of PFOA, they all suffer from an increased risk of disease that is different from the general background population at large. In clinical medicine, whenever a patient is at increased risk for a specific disease we alter our care so that we are more vigilant and attentive in an attempt to diagnose that disease early. Thus, patients at increased risk for a disease are no longer provided "routine" medical care; instead, they are provided care consistent with the increased risk. Standards routinely acknowledge the potential for additional testing or more frequent testing, including more frequent testing conducted at different periodicities than what might otherwise be recommended in the absence of the increased risk. Further, when the increased risk is the result of exposure to a toxic substance that is not readily understood in the medical community at large, as is the case with PFOA, we involve medical professionals who are knowledgeable about the toxicity of the substance and the health effects associated with exposure.

[32] This observation of the actual outcome of this inappropriate exercise by Dr. Guzelian should not be read as a criticism of Vermont clinicians, who care for the handful of patients whose records Dr. Guzelian has referenced.

With the above in mind, members of the Bennington Exposure Class will not get adequate evaluation and treatment unless they are provided the opportunity to participate in the proposed Bennington medical monitoring program. The proposed monitoring program was designed to meet the heightened clinical needs of Exposure Class members discussed above resulting from this populations' above-background exposure to PFOA in a manner consistent with accepted recommendations for exposed populations. And, to reiterate a response already made, the above-background exposure is in the range of serum concentrations that have been associated with the deleterious effects of PFOA that I have cited and that reviewing agencies acknowledged in their deliberations. The threshold for inclusion is a health based standard. As a result, the proposed Bennington monitoring and clinical testing protocol is inherently different from what a participating class member would receive in the course of routine preventive medical care. See Ex. B also attached (table comparing USPTFS recommendations to Bennington medical monitoring program recommendations). This exhibit shows clear and distinct differences between the proposed plan and one of the common general guidelines. Specifically, my proposed monitoring plan differs from the routine medical care in at least the following respects:

(1) Frequency of Testing: The frequency of the clinical testing recommended in my monitoring program, i.e., yearly testing, differs from that recommended in routine screening guidelines, including screening guidelines for the PFOA-related diseases for which the members of the Exposure Class are at an increased risk.

(2) Periodicity of Testing: The periodicity and initiation of the clinical testing recommended in the monitoring program, i.e., the age of initiation of screening, was modified to provide for earlier testing to account for the increased risk of disease which this population suffers from.

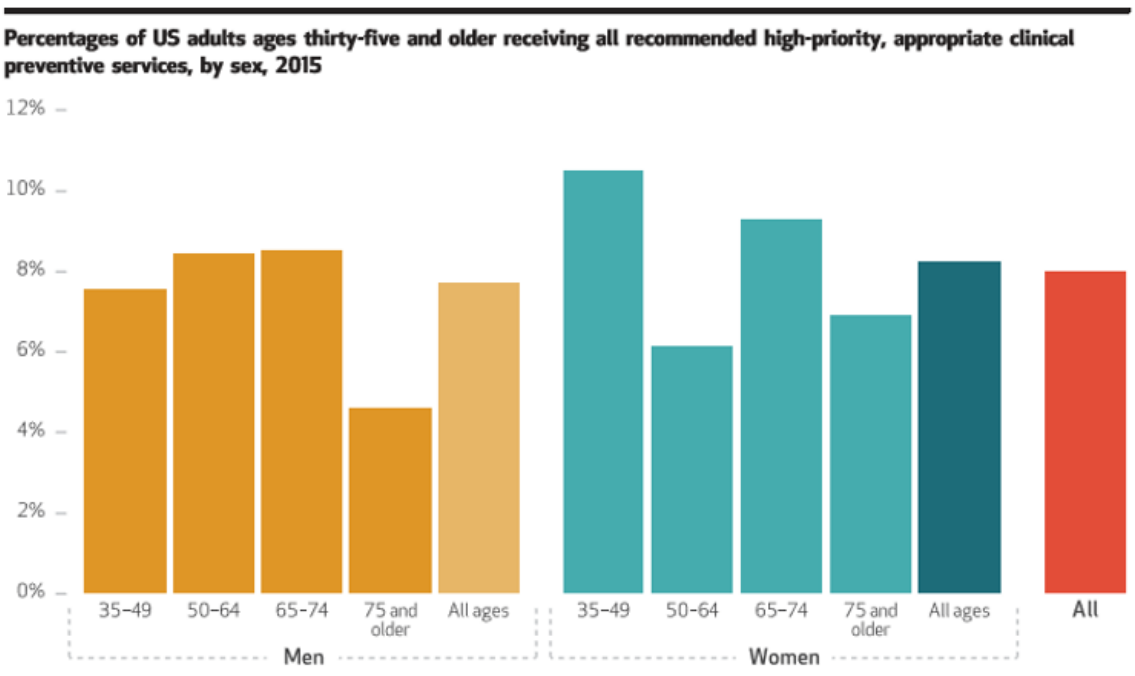
(3) Comprehensive Nature of Testing by Knowledgeable Medical Professionals: In addition to receiving clinical tests more frequently and at earlier intervals, participating Class Members will receive the full battery of clinical tests on a yearly basis, administered by physicians and staff trained in, and knowledgeable of, the health risks associated with exposure to elevated levels of PFOA, and the monitoring program as a whole will be overseen by a knowledgeable expert panel (epidemiologist and clinician) who will perform important program oversight functions.

This latter point is important because, as demonstrated by excerpts of the deposition testimony of the named plaintiffs set forth in Ex. C attached hereto, local Bennington physicians (understandably) are sometimes, but not always, knowledgeable as to the toxicity of PFOA or the diseases associated with exposure to elevated levels of PFOA. This is not surprising, as this is still highly-specialized information, and nationally most clinicians are not yet familiar with this class of emerging toxins or the demonstrated, already known toxicity. It is therefore unpredictable that Bennington clinicians will make appropriate recommendations as to modified plans of preventive care that, amongst other things, test earlier and more frequently in order to detect these diseases early. Some of the clinicians do seem knowledgeable concerning some of the health outcomes appropriate for monitoring; however, based on my review of Ex. C, there is evidence that some, but not all, of the named plaintiffs got some (but not all) of the recommended clinical tests included in my clinical testing protocol. This is the predictable outcome in the absence of a designed program, and, again, this is not any sort of criticism of the Bennington medical community.

(4) Lack of Preventive Screening during Routine Care: In his report, Dr. Guzelian makes the following fundamentally flawed assumption: “It is presumed that each plaintiff will follow the usual protocols for ordinary preventive medical care appropriate for a person in his or

her circumstances ….” (Guzelian, at 57). This assumption of compliance with recommended preventive testing protocols, and thus duplicative care through medical monitoring, is at odds with the literature in two distinct and important ways. First, it is misleading and at odds with the medical literature even for the population who are not in a special disease class and who do not deserve additional environmental consideration, as in fact about 8% of US adults receive care consistent with full compliance with preventive medicine recommendations (Borsky et al. 2018). Below is a graphic of the % of U.S. adults (35 and older) receiving all recommended and appropriate clinical preventive services, taking into account both testing and interventions:

Figure 2. From Borsky et al.



SOURCE Authors' analysis of data from the Preventive Services Self-Administered Questionnaire portion of the 2014 Medical Expenditure Panel Survey (fielded in 2015). **NOTES** Adults are noninstitutionalized civilians. The fifteen services are discussed in the text and listed by age-sex group in appendix B (see note 6 in text). Differences are not significant (men versus women: $p = 0.72$; by age among men: $p = 0.60$; by age among women: $p = 0.13$). Selected 95% confidence intervals and p values are in the text.

(Borsky et al. 2018). Second, Dr. Guzelian's assumption of duplicative care is fundamentally flawed as I did not propose medical monitoring in this population because of well-known gaps in

the delivery of preventive medicine services; rather, I am merely noting that the facile assumption that they are routinely delivered is in conflict with substantive evidence. For other than lipid testing, the disease outcomes we have selected for monitoring are not yet the target of routine preventive care in the absence of elevated risk. And, the targets of elevated risk following PFOA exposure is not current common clinical knowledge, and the substantial effort put into considering the risks and benefits of each elements of a testing protocol are not something that should be expected to occur in a typical 15-minute office visit. Thus, Dr. Guzelian is both assuming that needed monitoring will occur and actively seeking to prevent its occurrence. Virtually all guidelines acknowledge the difference between medical monitoring for populations at increased risk and preventive medicine recommendations for the entire population, as the latter is not designed to address coherent populations with environmental sources of increased risk.

Consistent with the guidance for excess environmental risk provided by ATSDR in community settings and by OSHA in work settings, I have proposed a unique, useful and non-duplicative monitoring protocol, consisting of monitoring survey questions, laboratory tests, and physical findings (in the case of home monitoring of blood pressure during pregnancy). Further, as demonstrated by Ex. B, even when members of the proposed class go to their physician with specific concerns about exposure, they receive a variable or limited and unpredictable set of the testing I have proposed in my monitoring program. This is as one would expect from busy clinicians who do not and cannot follow the vast medical specialty literature in multiple fields. Thus, the goal of my monitoring program is to make the testing consistent, and not ad hoc, as it currently is.

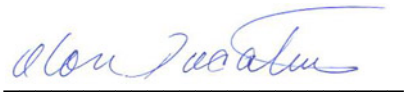
There is very little potential for duplication in the recommendations I have included in my proposed monitoring program. Where a preventive clinical test recommendation already exists --

for example, lipid testing, which is recommended at some point for all individuals – the proposed monitoring program is designed to introduce testing at an earlier date in proportion to the increased risk, and with increased follow-up. And, the remainder of the program very clearly recommends testing for specific risks which would not otherwise be received until participating class members presented at their clinicians' office with symptomatic and irreversible (or less reversible) disease.

Compensation

I charge $450 per hour for my time in preparing this report.

This the 1st day of August, 2018.



Alan Ducatman, M.D.

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EXHIBIT A

INTERNATIONAL CLASSIFICATION OF DISEASE CODES
VERSION 10

Clinical Test	Condition Sought	ICD Code
In-Home Blood Pressure	Gestational Hypertension Unspecified Preeclampsia	O13 O13.9 O14
Medical Monitoring Laboratory Test		
ALT, AST, GGT, Bilirubin	Fatty (change of) liver, NOS Or- Fatty liver with inflammation added ± Etiology Considered: Toxic Alternative: Liver Disease, unspecified	K76.0 K75.8 K71 & K71.9 K76.9
Cholesterol & LDL Cholesterol	Hypercholesterolemia Hyperlipoproteinemia LDL-type Mixed type hyperlipidemia	E78.00 E78.00 E78.2
TSH	Thyroid disease unspecified Other hypothyroidism ± Etiology considered ± Pregnancy considered	E07.9 E03 E03.2 O99.28O
Uric Acid	Hyperuricemia (without arthritis or tophi) Gout ± Etiology considered – other gout Gout, unspecified Calculus (stone)	E79.0 M10.0 M10.4 M10.9 N20.0-20.2
Urinalysis	Hematuria, NOS Calculus (stone) Malignant neoplasm of kidney	R31 N20.0-20.2 C64-65

EXHIBIT B

Disease	**USPSTF Recommendation**[1]	**MMP Recommendation**
Kidney Cancer	N/A	Yearly survey and diagnostic monitoring (urinalysis) for class members 18 years and older.
Testicular Cancer	Recommends against screening for testicular cancer in adolescent or adult men.	Yearly survey monitoring and optional clinical monitoring (physical examination) for all male class members 15 years and older.
Pregnancy Induced Hypertension	N/A	Yearly survey monitoring for female program participants of child rearing age; consultation with program physician for participants who become pregnant, including blood pressure cuff for at home monitoring for pregnant class members of 20 weeks or more.
Shortened Duration of Breast Feeding	Recommends providing counseling during pregnancy and after birth to support breastfeeding.	Consultation with program physician for any pregnant class member, and communication from the program physician with the participant's obstetrician regarding increased risk of complications.
Thyroid Disease (During Pregnancy)	N/A	Yearly survey monitoring for female program participants of child rearing age and consultation with program physician for any pregnant class member, and communication from the program physician with the participant's obstetrician regarding increased risk of complications
Thyroid Disease (Non-Pregnancy)	Recommends against screening for thyroid dysfunction in non-pregnant, asymptomatic adults	Yearly survey and clinical testing for all class members 12 years and older.
Liver Function Abnormalities & Non-Alcoholic Fatty Liver Disease	N/A	Yearly survey and clinical testing (blood testing) for all class members 12 years and older.
Hyperlipidemia	Recommends screening adult males 35 years and older and adult women (who show risk of heart disease) 45 years and older.	Annual survey and clinical testing (blood testing) for all class members 12 years and older.
Uric Acid Abnormalities & Gout	N/A	Annual survey and clinical testing (blood testing) for all class members 18 years and older.
Ulcerative Colitis	N/A	Annual survey monitoring for all class members 18 years and older.

[1] Available at *Published Recommendations*, U.S. Preventative Serv. Task Force, https://www.uspreventiveservicestaskforce.org/BrowseRec/Index/browse-recommendations.

EXHIBIT C